d) contacting said bacteria with said prodrug in a medium;

e) separating from said medium bacteriophage particles released by lysis of host bacteria;

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f) analyzing the genotype of said released bateriophage for the nucleic acid encoding the enzyme, or functional fragment thereof; and

g) cloning the nucleic acid of the released bacteriophage particles that encode the enzyme or enzyme fragment.

REMARKS

The specification has been amended to provide priority information. No new matter has been added.

By way of this amendment, claims 1 - 19 have been amended and new claims 20 and 21 are added. No new matter has been added.

Pursuant to 37 C.F.R. §1.121(c)(1)(ii), marked up versions of claims 1 - 19, showing all changes relative to the previous version of each, appear on separate sheets appended to this response.

Upon entry of this amendment claims 1 - 20 will be pending.

An Abstract is provided herewith.

Also provided herewith is a Sequence Listing of the sequences that appear in the application in paper copy and on diskette in computer readable form. The information recorded in the computer readable form is identical to the paper copy of the Sequence Listing.

Conclusion

Applicant respectfully submits that claims 1 - 21 are in condition for allowance. Applicant respectfully requests early notification of the same. If a telephonic interview would be helpful, the Examiner is asked to call the undersigned at 215-557-5901.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned **"Version with markings to show changes made."**

Respectfully submitted,

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Marked up versions of claims 1 - 19, which are amended herein, showing all of the changes relative to the previous version of each.

1 (Amended). A method of [selection of] selecting a nucleic acid encoding an enzyme that is capable of converting a prodrug to its active drug form comprising the steps of:

a) contacting a population of bacteria transformed with a bacteriophage library with a prodrug in a medium, wherein[;]:

i) the transformed bacteria are in the lysogenic state, and

ii) when converted to its active drug form, the prodrug causes activation of the proteolytic activity of bacterial RecA and lysis of the bacteria;

b) separating bacteriophage particles released by lysis of the bacteria from said medium[,]; and

c) analysing the genotype of said [separated] released bacteriophage particles for a nucleic acid encoding the enzyme.

2 (Amended). A method [for selection] of selecting a nucleic acid encoding an enzyme capable of converting a prodrug to its active drug form comprising the steps of:

a) introducing a library of genes into bacteriophage to form a bacteriophage library;

b) infecting a population of bacteria with said bacteriophage library;

c) selecting said infected bacteria for bacteria in which the lysogenic state has been established;

d) contacting said bacteria with said prodrug in a medium;

e) separating from said medium bacteriophage particles released by lysis of host bacteria; and

f) analysing the genotype of said [selected] released [bacteriaphage] bacteriophage for the nucleic acid encoding the enzyme;

wherein said prodrug causes activation of the proteolytic activity of bacterial RecA when converted to its active drug form.

3 (Amended). [A] The method [according to] of claim 1 or claim 2, wherein the steps are repeated in at least one cycle.

4 (Amended). [A] The method [according to any one of the preceding claims] of claim 1 or 2, wherein the [DNA sequence] genotype of said released bacteriophage particles is analysed by DNA sequencing.

5 (Amended). [A] The method [according to any one of the preceding claims] of claim 1 or 2, wherein said bacteriophage carry a gene encoding antibiotic resistance or other selectable marker.

6 (Amended). [A] The method [according to any one of the preceding claims] of claim 1 or 2, wherein said enzyme is selected from the group consisting of nitroreductase, flavin reductase, DT-diaphorase, thymidine kinase, cytosine deaminase, [or a] and purine nucleoside phosphorylase.

7 (Amended). [A] The method [according to any one of the preceding claims] of claim 1 or 2, wherein said prodrug is selected from the group consisting of CB1954, SN 23862, 2-[N,N-bis(2-iodoethyl)amino]-3,5-dinitrobenzamide, 5-fluorocytosine, acyclovir, ganciclovir, [or] and 6-methyl-9-(2-deoxy-β-D-erythro-pentofuranosyl) purine.

8 (Amended). [A] The method [according to any one of the preceding claims] of claim 1 or 2, wherein said [temperate] bacteriophage is the bacteriophage lambda or a lambda derivative.

9 (Amended). [A] The method [according to any one of the preceding claims] of claim 2, wherein said gene library comprises genes encoding variants of a single enzyme.

10 (Amended). [A] The method [according to] of claim 9, wherein said variants comprise amino acid deletions[,] and/or insertions and/or substitutions from the wild type enzyme.

11 (Amended). [A] The method [according to] of claim 9 [or 10], wherein said genes encoding said variants are generated by DNA shuffling, random mutagenesis, or PCR shuffling.

12 (Amended). [A] The method [according to any one of the preceding claims] of claim 1 or 2, wherein said activity of said bacterial RecA protein is caused by the generation of single-stranded DNA in the bacterium.

13 (Amended). [A] The method [according to] of claim 12, wherein said single-stranded DNA is generated as a consequence of the enzymatic conversion of the prodrug to its active drug form.

14 (Amended). [A] The method [according to] of claim [13] 12, wherein said single-stranded DNA [arises] is generated as a result of a break in one or both strands of the DNA, a cytotoxic lesion, a DNA crosslink or a monovalent DNA adduct, or by inhibition of the progress of DNA replication [by any other means].

15 (Amended). [A] The method [according to any one of the preceding claims] of claim 1 or 2, wherein said enzyme comprises nitroreductase and said prodrug comprises CB1954.

16 (Amended). [A] The method [according to any one of the preceding claims] of claim 1 or 2, wherein said bacteriophage [vector] is λJG3J1.

17 (Amended). [A] The method [according to any one of the preceding claims] of claim 1 or 2, wherein said [bacterium is of the] bacteria are *E. coli* strain C600*Hfl*.

18 (Amended). A nucleic acid molecule encoding a catalytic enzyme or enzyme fragment isolated according to the method [of any one of the preceding claims] of claim 20 or 21.

19 (Amended). A [nucleic acid molecule encoding a] catalytic enzyme or enzyme fragment [according to] encoded by the nucleic acid molecule of claim 18.